Thermosensitive Behavior of Poly(ethylene oxide)–Poly[bis(methoxyethoxyethoxy)- phosphazene] Block Copolymers

Youngkyu Chang, Eric S. Powell, Harry R. Allcock, Sang Mi Park, and Chulhee Kim

Macromolecules, 2003, 36 (7), 2568-2570 • DOI: 10.1021/ma021490d

Downloaded from http://pubs.acs.org on January 20, 2009

More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 6 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article
Thermosensitive Behavior of Poly(ethylene oxide)-Poly[bis(methoxyethoxyethoxy)phosphazene] Block Copolymers

Youngkyu Chang, Eric S. Powell, and Harry R. Allcock*

Department of Chemistry, The Pennsylvania State University, 152 Davey Laboratory, University Park, Pennsylvania 16802

Sang Mi Park and Chulhee Kim*

Hyperstructured Organic Materials Research Center, Department of Polymer Science and Engineering, Inha University, Inchon 402-751, Korea

Introduction

Thermosensitive polymers have attracted much attention for applications such as drug delivery, membranes, and cell culture. The lower critical solution temperature (LCST) is the temperature at which polymers in aqueous solutions or hydrogels undergo a transition from a soluble to an insoluble or opaque state or from a swollen hydrogel to a contract form as the temperature is increased. Several polymers, including poly[bis(methoxyethoxyethoxy)phosphazene] (MEEP), poly(N-substituted acrylamide), and poly(ethylene glycol)–poly(propylene glycol)–poly(ethylene glycol) triblock copolymers, are known for their LCST transition behavior. MEEP has a well-defined LCST at 80 °C, and hydrogels of this polymer, formed through γ-ray cross-linking, show promise for use in biomedical applications. The thermally induced aggregation behavior of these water-soluble diblock copolymers was investigated using UV/vis spectroscopy and dynamic light scattering (DLS). In addition, the water swelling behavior and temperature dependence of a copolymer with a molar PEO:MEEP ratio of 1.49 were studied after γ-ray cross-linking.

Experimental Section

Polymer Synthesis. PEO-block-MEEP copolymers were prepared from CH3–POE–NH2 using a procedure described previously in the literature. The copolymerization mixture with NaOCH2CH2OCH2CH2OCH3 gave the phosphoranimine NSiMe3. This PCl5-induced polymerization allows the production of a variety of polymeric phosphazene systems with controlled molecular weights and architectures, including block copolymers. The formation of block copolymers allows for an adjustment to be made to the physical properties that are characteristic of the component homopolymers. It seemed possible that the thermal sensitivity of the LCST of MEEP-type polyphosphazenes, as well as the water swelling behavior, might be tuned through the incorporation of an organic polymer block such as poly(ethylene oxide) (PEO). Here, we report the synthesis of potentially biocompatible and thermosensitive PEO–MEEP block copolymers through the PCl5-induced, controlled cationic polymerization of phosphoranimines.

Results and Discussion

Block copolymers containing a biocompatible, hydrophilic PEO segment and a thermosensitive MEEP portion were synthesized via the controlled, PCl5-induced, cationic polymerization of phosphoranimines at ambient temperature, using amine-terminated PEO as a starting material (Scheme 1). The macroinitiator CH3–POE–NH–P(OCH2CF3)2=NSiMe3 was synthesized from amine-terminated PEO (Mn = 5400 g/mol, ShearWater) and Br–P(OCH2CF3)2=NSiMe3. Reaction of 4 with 2 equiv of PCl5 yielded the cationic species CH3–POE–NH–P(OCH2CF3)2=PCl5=NSiMe3 (5). Subsequent addition of varying amounts of Cl3P=NSiMe3 to 5 allowed the preparation of PEO-block-poly(dichlorophosphazene) copolymers with controllable phosphazene block lengths. Further treatment of this reaction mixture with NaOCH2CH2OCH2CH2OCH3 gave PEO-block-MEEP copolymers through the macromolecular replacement of labile chlorine atoms. A series of block copolymers were prepared by varying the length of the MEEP block, while the length of the PEO block remained constant. Gel permeation chromatography was used to measure average molecular weights and polydispersities, and these were compared to values calculated using 1H NMR (Table 1).

Aqueous Phase Behavior. MEEP is known to undergo an LCST transition at 80 °C in water. Thus, the water-soluble PEO-block-MEEP copolymers synthesized in this work were expected to show thermosensitive self-organization in water associated with the LCST behavior of the MEEP block. The temperature-dependent phase transitions of aqueous PEO-block-MEEP solutions were monitored by observing the changes of transmittance at 450 nm, as shown in Figure 1. Aqueous solutions of polymer 8 (molar PEO:MEEP

---

The text contains information about the synthesis and properties of block copolymers containing PEO and MEEP segments, focusing on their thermosensitive behavior and potential applications in biomedical fields.
the aggregates became soluble again. The self-aggregation process was completely reversible, and the aggregates became soluble above these temperatures. Light scattering measurements showed that the hydrodynamic radius, $R_h$, of the self-aggregates increased from 270 to 540 nm (from 460% to 36%), probably related to the LCST characteristics of the MEEP block. The block copolymers described here were expected to show lower cross-link densities than MEEP itself as a result of a smaller number of cross-linkable sites per chain. However, higher water uptake and swelling values might be expected because of the presence of the hydrophilic PEO blocks in the copolymer. Four samples of PEO-block-MEEP copolymers (Table 1), varying in MEEP block lengths, were irradiated with $60\text{Co}$-$\gamma$-radiation (20 Mrad radiation dose). After cross-linking, a film of polymer 11 (PEO:MEEP ratio of 1:4.9) showed good mechanical strength, but polymers 8, 9, and 10 (PEO:MEEP ratios of 1:0.49, 1:1.2, and 1:2.7, respectively) did not form free-standing films. This could be due to the larger proportion of PEO, relative to MEEP, found in these particular systems. Our previous study revealed that PEO (M$_n$ = 5000) did not cross-link when exposed to the same radiation dosage as the copolymers discussed here. Hydrogels of polymer 11 showed uniform swelling behavior in water and a swelling ratio larger than that of the MEEP homopolymer. The water uptake value of polymer 11 was 460%, while that of MEEP was 300%, with both having been cross-linked with a 20 Mrad radiation dose. The water swelling behavior of the hydrogel formed from polymer 11 was also examined over a wide temperature range to ascertain its usefulness for biomedical applications. As shown in Figure 2, this hydrogel showed relatively constant water absorption values in the range 25–50 °C. However, a dramatic decrease in water swelling (from 460% to 36%), probably related to the LCST behavior of the MEEP block, was detected above 50 °C. In addition, the initial transition temperature for the...
hydrogel of polymer \(11\) is lower than the phase transition temperature of the aqueous solutions of the corresponding un-cross-linked block copolymer. This suggests that the bulk state of the cross-linked hydrogel is more sensitive to changes in temperature than the un-cross-linked block copolymer solution. The water swelling behavior was reversible, and the hydrogel retained its original shape after the study.

In conclusion, PEO-block-MEEP copolymers were synthesized using the controlled cationic polymerization of phosphoranimines. The block copolymers synthesized had molar PEO:MEEP ratios of 1:0.49, 1:1.2, 1:2.7, and 1:4.9, with the length of the PEO segment held constant at 5400 g/mol. The self-aggregation characteristics of the block copolymers in water have been investigated by using UV/vis spectroscopy and dynamic light scattering. These studies revealed a temperature dependence of the hydrodynamic radii of self-aggregates due to the LCST behavior of the MEEP block. A hydrogel of a block copolymer with a molar PEO:MEEP ratio of 1:4.9 was also synthesized, and its temperature dependency was studied. This hydrogel exhibited larger water uptake values than those of MEEP homopolymer, which is probably due to the hydrophilic nature of the PEO blocks. The thermosensitive phase-transition and water-swelling behavior of the PEO-block-MEEP copolymers was examined as the first step toward their utilization as potential biomaterials and for uses in both temperature-responsive membranes and delivery matrices.

Acknowledgment. This work was supported by the National Science Foundation through Grant CHE-0211638. C.K. thanks the Korea Research Foundation (2001-041-E00333) for their support.

References and Notes


